

NEUROSTIMULATION: A NOVEL APPROACH TO TREATING THE SIGNS AND SYMPTOMS OF DRY EYE

A device in clinical study could lead to new understanding of dry eye as a neuronal disease.

BY JOHN BERDAHL, MD



I get excited about innovations that approach problems from unique perspectives, especially if these new ideas have the potential to meaningfully change patients' care. Of course, novelty is only part of the equation. Because a new device or technology must be safe and effective to be useful, I tend to balance my excitement about new

technologies with a healthy dose of skepticism.

When we at Vance Thompson Vision were approached about doing research on OD-01 (Allergan), a device with probes placed in the nose to stimulate the lacrimal glands to produce tears, I was intrigued by its potential application to the problem of dry eye disease (DED). The role of inflammation in DED, whether the disease is aqueous deficient or evaporative, is well known, yet therapies directed at this target are often less than optimal. Approaching DED from a neurologic perspective represents an entirely new way of treating this insidious problem.

A device that could actually increase tear production, thus supplying the dry eye with improved lubrication, seemed like a far-fetched idea when I first heard about OD-01, or at least it seemed like the approach might not be much better than an artificial tear. The device was originally developed by Oculieve, a development-stage medical device company that was acquired by Allergan last year. Aware that the device could ultimately fail but feeling like it would be safe, we decided to participate in early studies of the technology.

The early results with this device have convinced me that the OD-01 could be an impressive solution for DED patients. Although many questions remain to be answered and regulatory hurdles are still to be negotiated, it appears that neurostimulation of the lacrimal glands may address the acute condition in DED.

“OD-01 is a noninvasive nasal neurostimulation device that increases tear production in patients with DED.”

NEUROSTIMULATION

OD-01 is a noninvasive nasal neurostimulation device that increases tear production in patients with DED. Inserted through the nose, the device has two prongs that contact the ophthalmic branch of the trigeminal nerve (5V1) and then stimulate the cranial nerve VII; the latter innervates the lacrimal glands. Low-level electrical stimulation from the device functions to stimulate the lacrimal gland into greater activity, resulting in increased tear production.

The exact mechanism of action of OD-01 is still under investigation, because there is some suggestion that the device may produce long-term effects. One proposed mechanism is that neurostimulation works to kick-start the system through some form of lacrimal gland remodeling.

Although investigation continues on what makes the OD-01 effective, clinical results show that the device yields positive benefits in the signs and symptoms of DED in many patients. I recall a follow-up visit with the first patient I treated with the device. After a week of use, I asked her whether anything had changed since enrollment in the clinical study. She told me that she was now able to read a book at night for the first time in

PIVOTAL TRIALS OF OCULEVE MET PRIMARY, SECONDARY ENDPOINTS

Allergan announced that two pivotal trials of the Oculeve Intranasal Tear Neurostimulator, OCUN-009 and OCUN-010, each met their primary and secondary efficacy endpoints. With these new results, a premarket submission for the device is on track to be submitted to the FDA in the second half of 2016, a news release from the company stated.

The handheld stimulator (and daily disposable tips) increases tear production upon stimulation in patients with dry eye disease (DED) owing to decreased tear production. Several Oculeve clinical studies have been completed, with more than 200 adult patients showing positive safety and efficacy of the device, Allergan stated.

"We are excited with the outcome of these two sets of pivotal data," said David Nicholson, chief R&D officer at Allergan. "The Oculeve Intranasal Tear Neurostimulator is a novel approach and has the potential to help patients suffering from [DED] by increasing their natural tears. This device is part of Allergan's strong eye care development pipeline and will complement our leading [DED] treatment Restasis. This is a major step forward in providing a promising new option for eye care professionals and their patients with [DED]."

7 years. To me, that is a dramatic result. Although that is an anecdotal account of a subjective impression of efficacy, I can report that several other patients in the trial described similar benefits. We investigators may still be working on understanding why OD-01 works, but patients seem to be happy with the results they are getting with the device in clinical trials.

To date, the OD-01 has been evaluated in more than 400 patients as part of seven trials, including pivotal trials, and all have hit their primary endpoints and had positive safety results, according to Allergan. The company purchased Oculeve last year with the intention of continuing the development of the device. Allergan plans to submit the device to the FDA for approval this summer.

CONCLUSION

The application of electrical stimulation in this setting opens a new category of treating DED—and, potentially, of understanding DED—as a neuronal disease. Electrotherapy has been used in numerous other settings for pain control, rehabilitation, and stimulation, and there are parallels to DED. DED symptoms can include pain, the tear film needs to be rehabilitated, and stimulation of the nerves associated with the lacrimal gland may be relevant to produce a long-term benefit. There is much to be done in relation to understanding the science of this approach to DED management. For

ABOUT THE STUDIES

The OCUN-009 study is a prospective, randomized, controlled, double-masked, multicenter, crossover trial in which participants used an active device and two control applications. The primary effectiveness endpoint of increased tear production over basal during intranasal application as measured by Schirmer score compared to both controls was met. The OCUN-010 study design is a prospective, single-arm, multicenter, open-label clinical trial in which participants used the Oculeve Intranasal Tear Neurostimulator to stimulate tear production for 180 days. The primary effectiveness endpoint of increased tear production as measured by Schirmer score during application of the device compared with basal Schirmer score at day 180 was met. Secondary endpoints of increased tear production as measured by Schirmer score during application of the device compared with basal Schirmer score at days 0, 7, 30, and 90 were also met.

CONCLUSION

All device-related adverse events were mild in nature. There were no device-related serious adverse events. No patient discontinued treatment due to adverse events.

now, a positive is that patients receiving the treatment have been happy with it.

DED is a problem that affects many patients, and great solutions are lacking. An army of drugs aiming to restore the health of the tear film line the shelves of drugstores, but these products are not always effective. Often, the amount of effort the patient has to put into rehabilitating the tear film with these remedies is not worth it. Applying warm compresses once or twice a day, taking omega-3 fatty acid dietary supplements, using a medication or two, avoiding sleeping under a ceiling fan, humidifying the environment, undergoing expensive office-based procedures that are not covered by insurance—many of the interventions doctors typically recommend to address DED can be onerous for patients, especially those with severe disease. The early results I have observed with OD-01 make me cautiously optimistic that this approach to treatment could offer a novel, safe, and effective solution to an insidious problem. ■

John Berdahl, MD

- clinician and researcher, Vance Thompson Vision, Sioux Falls, South Dakota
- johnberdahl@gmail.com
- financial disclosure: consultant to Allergan